

Prevention of Dental Caries-Measures beyond Fluoride

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Abstract

Dental caries is one of the most common infectious microbial diseases. It is rightly said that prevention is better than cure. Various steps in prevention of dental caries have been taken, fluoride being the most common among them. Various non-fluoride agents are also present which helps in prevention of dental caries. Various agents like, arginine, plant extracts, sucrose free polyol gums, probiotics, novamin, Dentrifrices, antimicrobials, CPP- ACP etc are commonly used in prevention of dental caries. This paper reviews about these non-fluoride agents in the prevention of dental caries.

Keywords: Dental Caries; Non fluoride agents; Prevention

Introduction

Dental caries is one of the most common preventable childhood disease; people are susceptible to this ailment throughout the lifetime [1]. Data from the National Health and Nutrition Examination Survey (NHANES) conducted between 1999 and 2004 revealed that 28 percent of children ranging from 2 to 5 years of age had one or more primary tooth affected by dental caries and 51 percent of children had one or more primary tooth affected by age 6 to 11. In the permanent dentition, 10 percent of children aged 6 to 8 had dental caries and 51 percent of children were affected by age 12 to 15 [2]. The preventive care providers have the intention for prevention beyond the scope of providing hygiene therapy and oral hygiene instructions. Dental decay is mainly due to demineralization which is caused by acids produced by bacteria, particularly mutans Streptococci and possibly lactobacilli that ferment dietary carbohydrates. This occurs within a bacteria-laden gelatinous material called dental plaque that adheres to tooth surfaces and becomes colonized by bacteria. Thus, caries results from the interplay of three main factors over time: dietary carbohydrates, cariogenic bacteria within dental plaque, and susceptible hard tooth surfaces [3]. The use of fluoridated toothpastes [4], other topically applied fluorides [5], fluoridated municipal water [6] and pit and fissure sealants [7,8] along with dietary improvement remain mainstays of caries management. These modalities, which are based on high quality evidence, are the first choice for prevention and control of dental caries. Fluoride's anti-caries efficacy is well-proven and may arise from multiple modes of action, i.e., inhibition of tooth demineralization, promotion of incipient lesion remineralization, and perhaps, antibacterial effects on cariogenic bacteria [9]. Clinical evidence would suggest that increasing the concentration of fluoride above the conventional level of 1000 or 1500 ppm in dentifrices will give an increased benefit although there would appear to be something of a law of diminishing returns [10]. Although fluoride is highly effective on smooth-surface caries, its effect would seem to be more limited on pit and fissure caries, and these lesions tend to dominate the caries experience of developed countries currently enjoying the benefits of fluoride. Apart from fluoride, dental health education programme, diet counselling, oral hygiene measures like dentifrices, different brushing technique are also used in prevention of dental caries. Various anti plaque agents, and other agents like enzymes have been effectively used as prevention of dental caries. From the 1930's when the researches came to know the anti-caries effect of the fluoride, many gargantuan water fluoridation program have been implicated, but these programs has shown to be successful only in attaining a 50% caries reduction but none of them

was able to contain the caries process [11]. Since 1970's researches started to search for non-fluoride agents for the prevention of dental caries [12]. Non-fluoride agents may serve as adjunctive therapeutics for preventing, arresting or even reversing dental caries. The objective of this paper is to present a complete review of recent advances of various non-fluoridated caries preventing agents.

Recent Advances in Caries Prevention

Arginine

Arginine, a common amino acid found in saliva is broken down by oral plaque bacteria to acid neutralizing alkali. The production of acid by dental plaque is the direct cause of dental caries; it is noteworthy that increases in the proportions of aciduric organisms appear to occur at the expense of species that are less aciduric and generally associated with dental health; including *Streptococcus sanguinis* and *Streptococcus gordonii* [13-15]. Some of the less aciduric organisms associated with dental health derive protection from plaque acidification by hydrolysing urea or arginine to ammonia, either by expressing a urease enzyme or by the arginine deiminase system (ADS), respectively. Production of ammonia by oral bacteria can positively influence the balance between remineralization and demineralization of the tooth and may help to prevent the emergence of a cariogenic microflora [16-18]. Therefore, the capacity of oral biofilms to generate alkali appears to be a major caries-inhibiting factor [19]. Urea and arginine can be rapidly metabolized by oral bacteria to elicit a rise in environmental pH. A strong correlation between elevated levels of free arginine in saliva and caries resistance has also been revealed [20]. In addition, dental plaque of caries-resistant individuals has been shown to have higher pH values compared to the plaque of caries-susceptible individuals, and in part the increased pH has been correlated with elevated ammonia levels [21-33].

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Plant extracts

There is a global need for alternative prevention and treatment options and products for oral diseases that are safe, effective and economical. One such strategy would be to verify the enormous use of medicinal plants. A number of phytochemicals, including antibacterial agents have been derived from edible plants and demonstrate antibacterial properties against *Streptococcus mutans*.

Neem, *Azadirachta indica*: Wolinsky et al. [24] investigated the inhibitory effects of aqueous extracts from Neem upon bacterial aggregation, growth and adhesion to hydroxyapatite and production of insoluble glucan, which may effect *in vitro* plaque formation.

Tulsi, *Ocimum sanctum*: Tulsi, *Ocimum sanctum* is a plant of Indian origin and a time tested premier medicinal herb. The extract of tulsi is used to treat a variety of illnesses that include diabetes mellitus, arthritis, bronchitis and skin diseases. The antimicrobial property of tulsi has been tested against a variety of microorganisms like *Staphylococcus aureus*, *Klebsiella*, *Candida albicans*, *E. coli* and *proteus sp.* The antimicrobial activity of tulsi is attributed to its constituents namely ursolic acid and carvacrol. Agarwal et al. [25] in their study demonstrated an antimicrobial potential of tulsi extract at various concentrations and achieved maximum antimicrobial potential at 4% concentration level.

Prunus mume: *Prunus mume* is a common fruit in Asia, which has been used in traditional Chinese medicine. It is considered to be the potential candidate for developing an oral antimicrobial agent to control or prevent dental diseases associated with oral pathogenic bacteria like *Streptococcus mutans*, *S. sobrinus*, *S. mitis*, *S. sanguinis*, *Lactobacillus acidophilus*, *P. gingivalis*, *Aggregatibacter actinomycetem comitans* [26].

Green and black tea (*Camellia sinensis*): Various component in green and black tea (leaves of *Camellia sinensis*, [Theaceae]) notably simple catechins, have anticariogenic activity. These include: a direct bactericidal effect against *S. mutans* and *S. sobrinus*; prevention of bacterial adherence to teeth; inhibition of glucosyl transferase, thus limiting the biosynthesis of sticky glucan; inhibition of human and bacterial amylases. Ferrazzano et al. [27] concluded that the anti-cariogenic effect against alpha hemolytic streptococci by polyphenols from cocoa, coffee and tea suggest further possible application of these beverages in the prevention and pathogenesis of dental caries.

Hop plant (*Humulus lupulus*): Tagashira et al. [28] reported the inhibition of *S. Mutans* and other oral streptococci, by the antimicrobially active ingredients of hop plant. They found that all tested hop constituents inhibited the streptococci with minimum inhibitory concentration at pH 7.5 ranged from 2 to 50 µg/ml. Antimicrobial activity of hop constituents was greater than other plant products such as thymol, nerol, cinnamon oil, oil of clove, menthol and eucalyptol.

Oleic acid, Linoleic acid, epicatechin polymer (Cacao bean husk): These shows antimicrobial activity against planktonic cells of mutans Streptococci. It has an inhibitory effect on water-insoluble substances, polymer glucan synthesis, adherence, acid production by mutans streptococci. It also helps in reduction in plaque accumulation and caries development in rats infected with *S. mutans* or *S. sobrinus* [29,30].

Proanthocyanidins, phenolic acids, flavonols (Cranberry): These shows antimicrobial activity against biofilm cells of mutans

streptococci. It causes disruption of acidogenic/aciduric properties of planktonic and biofilm cells of *S. mutans*. It has inhibitory effects on Gtf activity and adherence by mutans Streptococci and causes reduction of formation of *S. mutans* biofilms and EPS content. Reduction in caries development in rats infected with *S. mutans* is also seen [31-33].

Apigenin and tt Farnesol: Apigenin and tt Farnesol are two naturally occurring agents that affect the development of cariogenic biofilms. Apigenin inhibits the activity of glucosyltransferases in solution and on the surface of saliva-coated hydroxyapatite beads and it was devoid of antibacterial activity. tt-Farnesol showed modest antibacterial activity against biofilms and its effects on glucosyltransferases were minimal [34]. It also enhances the cariostatic effectiveness of fluoride. The combination of these novel agents with fluoride may represent a potentially useful and an alternative approach to the current chemotherapeutic strategies to prevent this ubiquitous disease by reducing the expression of virulence of *S. mutans* without necessarily suppressing the resident oral flora [35].

Meswak chewing sticks (Twigs of *Salvadora persica*): These sticks embedded in agar or suspended above the agar plate had strong antibacterial effects against all tested bacteria. The antibacterial effect of suspended meswak sticks suggested the presence of volatile active antibacterial compound [36-39].

Propolis: Propolis is a natural beehive product, and cacao bean husk extracts have also shown significant antibacterial activity against *S. mutans* and/or *S. sobrinus in vitro* [29,38,39]. Propolis extract when used as a mouthwash exhibits an *in vivo* antimicrobial activity against *S. mutans* and might be used as an alternative measure to prevent dental caries [40]. Topical applications of chemically characterized Propolis extracts have also been shown to be highly effective in reducing the incidence and severity of smooth surface and sulcal caries in rats [39,41]. However, the cariostatic effects of propolis are highly variable depending on its chemical composition and geographical origin. There are many other reports in the literature concerning the antimicrobial activities that various plant extracts may have against cariogenic bacteria, although the majority of these studies provide limited or incomplete information due to the lack of chemical characterization of the extracts. However, there are a few exceptions. For example, Li et al. [42] have identified gallotannins from *Melaphis chinensis* and triterpenes (ceanothic acid and ceanothetic acid) from *Ceanothus americanus* as antimicrobial agents that harbor activity against mutans streptococci. Furthermore, a chemically characterized extract of *Galla chinensis* (containing gallic acid and methyl gallate) has been demonstrated to impede the growth of *S. mutans* and other caries-related organisms, including *Lactobacillus rhamnosus* and *Actinomyces naeslundii*, within biofilms [43]. Recently, established that naturally occurring phenolic compounds generally display antibacterial activity by disrupting the membrane lipid-protein interface as nonionic surface-active agents [44]. Ramakrishna et al. [38] studied various natural alternatives derived from plants and plant products and concluded that it can serve as a prevention and treatment option against cariogenic bacteria.

Chinese Licorice Root: A new cavity fighting herbal lollipop that contains a special herbal formula extracted from the Chinese licorice root can help to immobilize major organisms responsible for tooth decay. These orange flavoured herbal lollipops was discovered by microbiologist at the UCLA school of dentistry should be consumed twice a day- one in the morning after breakfast and another after professional teeth cleaning between two and four times a year.

Xylitol: A sweet alternative discovered in 1891 by German chemist

Emil Fischer. Dental benefits of xylitol were first recognized in Finland in 1970 using animal models. The first chewing gum developed with the aim of reducing caries and improving oral health was released in Finland in 1975 and in United States shortly after. Xylitol is not fermented by cariogenic plaque bacteria and thus does not lower the pH of the plaque. It reduces the accumulation of plaque on the surface of the tooth. It accumulates intracellularly in MS and inhibits the bacterial growth. Xylitol reduces MS by altering their metabolic pathways. It has long been known to have antibacterial properties, in particular to depress the proportion of *Streptococcus mutans* in plaque [45,46], and also to reduce its acidogenicity [47]. In addition, xylitol has been suggested to have an ability to inhibit enamel dissolution *in vitro* [48]. In clinical studies, xylitol chewing gums have, in general, been reported to inhibit the development of caries [49]. In children reporting caries experience, consumption of xylitol containing lozenges or hard candy reduces incidence of coronal caries [50-52]. For children below age two, in addition to the study that evaluated xylitol tablets, the xylitol-containing syrup among children in the Marshall Islands and reported a statistically significant difference in favor of xylitol syrup [53]. There is insufficient evidence that xylitol syrup prevents caries in children under 2 years of age. There is insufficient evidence regarding xylitol dentifrice as it contains other ingredients which might inhibit the production of dental caries [54,55].

Probiotics and replacement therapy: Probiotics are defined as live micro-organisms, principally bacteria, that are safe for human consumption and when ingested in sufficient quantities, have beneficial effect on human health, beyond basic nutrition [56]. First probiotic species to be introduced in research was *Lactobacillus acidophilus* by Hull et al. in 1984; followed by *Bifidobacterium bifidum* by Caglar et al. [57]. Probiotics have shown to influence immune system through several molecular mechanisms: In oral cavity, probiotics can create a biofilm, acting as a protective lining for oral tissues against oral diseases. Such a biofilm keeps bacterial pathogens off oral tissues by filling a space pathogens would invade in the absence of the biofilm; and competing with cariogenic bacteria and periodontal pathogens growth. The administration of probiotic lactobacilli (LGG) in milk to kindergarden children in Helsinki, Finland resulted in reduction of initial caries development. Comelli et al. [58] studied 23 dairy bacterial strains for the prevention of dental caries and reported that only two strains namely *Streptococcus thermophilus* and *Lactococcus lactis* were able to adhere to saliva-coated hydroxyapatite and were further successfully incorporated into a biofilm similar to the dental plaque. Recently it was shown that probiotic cheese reduced the prevalence of oral candida [59]. Cheese might be the ideal vehicle for administering probiotics to humans. Cheese enhances remineralization and prevents demineralization of enamel. Yogurt products containing *L. reuteri* showed a significant growth inhibitory effect against *S. mutans*, while yoghurts with lactobacilli other than *L. reuteri* did not show such inhibition. Residence time of probiotics in oral cavity after treatment withdrawal was studied by Caglar et al. [60]. A reduced *S. mutans* level was shown after a two-week use of a *L. reuteri*-enriched yogurt; effects were observed during use and for a few days after discontinuation. A loss of *L. reuteri* colonization was observed by Wolf et al. [61] two months after having discontinued probiotic use. Sucking a medical device containing the probiotic lozenge with *L. reuteri* once daily for 10 days reduced the levels of salivary mutans [62]. However it is unlikely that a permanent colonization occurs. Therefore, regular consumption of probiotic products is needed to maintain the preventive and therapeutic levels.

In addition to probiotics, another measure that competitively

reduces the pathogen composition in the oral flora has emerged with the advances in gene engineering and DNA recombination technology. This method is the so-called replacement therapy. Replacement therapy involves the use of a harmless effector strain that is permanently colonized in the host's microflora. This effector strain is designed to prevent the colonization or outgrowth of a particular pathogen. To prevent an infection using replacement therapy (recently referred to as probiotic therapy), a natural or genetically modified effector strain is used to intentionally colonize the sites in susceptible host tissues that are normally colonized by a pathogen. If the effector strain is better adapted than the pathogen, colonization or outgrowth of the pathogen will be prevented by blocking the attachment sites, by competing for essential nutrients, or via other mechanisms. As long as the effector strain persists as a resident of the indigenous flora, the host is protected potentially for an unlimited period of time. *S. mutans* strain BCS3-L1 is a genetically modified effector strain designed for use in replacement therapy to prevent dental caries. To be an effective effector strain, BCS3 L1 must satisfy four prerequisites: It must have a significantly reduced pathogenic potential to promote caries. It must persistently colonize the *S. mutans* sites, thereby preventing colonization by disease-causing strains whenever the host comes into contact with them. It must aggressively displace indigenous strains of *S. mutans* and allow previously infected subjects to be treated with replacement therapy. It must be safe and not make the host susceptible to other disease conditions. From a standpoint of replacement therapy for caries prevention, implantation of an effector strain would best be achieved in children immediately after tooth eruption and before the acquisition of a caries-inducing strain. A final aspect of replacement therapy safety is the requirement for controlled spread of the effector strain within the population. Mutacin 1140 up-production clearly provides a selective advantage to BCS3-L1 colonization. However, the minimum infectious dose has not been determined for this strain or any *S. mutans* strain in humans.

Novamin: Novamin falls into a newer category of bioactive glass-ceramic material that has been available since the 1960's as materials to help in bone repair. The active ingredient is a calcium sodium phosphosilicate that reacts when exposed to aqueous media, thus providing calcium and phosphate ions to the applied surface. Examples of Novamin powered technology include Oravive, a product from Natural Health Organics, which is a non-fluoridated, and non-prescription dentifrice containing 5% Novamin. Bioactive glasses have been tested under different clinical situations, such as having an antibacterial effect [63]. Novamin-containing dentifrice is statistically more effective than a placebo dentifrice [64]. One of these studies was done by and compared a dentifrice containing 5% Novamin and Fluoride (MFP) to a commercially available dentifrice in remineralization of subsurface carious lesions in human tooth enamel. It used confocal laser scanning microscopy (CLSM), which is able to distinguish between sound enamel and demineralized enamel using a fluorescent dye [65].

Dentifrices: Tooth-pastes are the valuable adjuncts to oral hygiene as they make brushing more pleasant and more effective. Many attempts have been made at various times to add-therapeutical agents with the object of interfering with oral flora, limiting plaque formation and making teeth more resistant to caries.

Chlorophyll: Chlorophyll was one of the earliest agents added to the paste and is still present in some tooth-pastes. Although *in vitro* tests showed that chlorophyll-containing tooth pastes limit bacterial growth, but clinical trials have not shown any anti- caries effects [12,66].

Ammoniated tooth-paste: This usually contains urea, and developed in an attempt to control the acid production in plaque. A numbers of clinical trials were carried out, but all gave very little positive or inconclusive results. Ammoniated pastes have been superseded by more effective agents, Anti-biotic toothpastes containing penicillin, triclosan or topical anti-biotic such as tyrothricin have also been tried. It was based on the assumption that if acidogenic bacteria are destroyed, caries will be controlled.

Anti-enzyme paste: These toothpastes were introduced on the basis that they interfere with enzyme systems of the bacteria and thus with their growth and function. Still their effectiveness has not been evaluated by clinical trials [12,66]. Various other dentrifices containing herbal products like neem, tulsi, clove oil, propolis are available which show beneficiary effect in preventing dental caries.

Antimicrobials: Typically antimicrobial agents target both supra-gingival plaque, and more importantly sub-gingival plaque buildup. Clinical decisions to deliver antimicrobial agents exist in a balance between delivering relevant and clinically measurable amounts, but at the same time not disrupting the natural ecology of the mouth which provides protection from opportunistic pathogens and the overgrowth of exogenous microbes.

Chlorhexidine: Currently mouthrinses that contain 0.12% chlorhexidine are marketed within the United States. Chlorhexidine is a broad spectrum antibiotic that kills Gram-positive and Gram-negative bacteria as well as yeasts at high concentrations. At lethal concentrations chlorhexidine causes irreparable damage to the cell membrane of target microbes, and at sub-lethal concentrations chlorhexidine can interfere with the sugar transport and acid production of the cariogenic streptococci strains, providing a bacteriostatic effect. Chlorhexidine is typically utilized because of its great retention within the plaque coated enamel surface, and studies report that 30% of the delivered chlorhexidine is retained in the mouth after use [67,68]. The efficacy of the chemical has come under scrutiny as some clinical trials have failed to produce significant level of caries reduction, and side effects such as staining and an altered taste sensation have been reported [69].

Triclosan is used to increase the ability of mouthwashes to bind to the oral mucosa, and thus be available for long period of time. Jenkins et al. compared the magnitude and duration of salivary bacterial count reduction produced by a single rinse of 0.2% triclosan, 1% sodium lauryl sulfate and 0.2% chlorhexidine mouthwashes. They found considerable reduction in bacterial count which remained significant for three hours with triclosan and for 7 hours with sodium lauryl sulfate and chlorhexidine [70]. The use of 0.3% triclosan mouth rinse showed significant reduction in salivary *Streptococcus mutans* count [71].

Essential oils: Essential oils have also been extensively studied for antimicrobial activity against caries-related bacteria. Essential oils derived from plants are typically a complex mixture of approximately 20-60 compounds that are in solution at various concentrations. Overall, the main chemical group is primarily composed of terpenoids, followed by aromatic and aliphatic constituents [72]. Thymol and eugenol inhibit the growth of a wide range of oral microorganisms including mutans streptococci [36,37].

Trace elements: Different trace elements has been investigated were zinc, tin, aluminium, copper, iron, strontium, barium, manganese and molybdenum, gold, lead etc. Aluminum, copper, and iron have the most commonly used as cariostatic agent, although each would probably have organo-leptic problems if used in oral care products as simple salts. Moreover, the toxicity of many metals like aluminum,

copper, barium molybdenum, would restrict the concentration at which they could be safely used [66,73].

CPP-ACP: Recent developments in the area of remineralization include casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) Dairy products such as milk, milk concentrates and cheese are recognized as non-cariogenic or cariostatic in several laboratory studies due to the presence of milk phosphoprotein, casein [74]. The casein phosphopeptides (CPP) are derived from casein by tryptic digestion. In 1987, Reynolds found that CPPs were incorporated into the intra-oral appliance plaque and were associated with a substantial increase in the plaque's content of calcium and phosphate [75]. All CPPs contain the sequence motif -Pse-Pse-Pse-Glu-Glu-, where Pse is a phosphoseryl residue. Through these multiple phosphoseryl residues, CPPs have a marked ability to stabilize calcium phosphate ions in solution and to form an amorphous calcium phosphate (ACP) complex, referred to as CPP-ACP [74,76]. The milk protein, CPP, stabilizes high concentrations of calcium phosphate ions in ACP solutions. The CPP-ACP is taken up by dental biofilms and localizes to the enamel surface as nanoparticles. Calcium, phosphate and fluoride from CPP-ACP, which are released during Acidogenic challenge, help to maintain the supersaturated state of these ions in the biofilm and so promote remineralization over demineralization [77]. Several randomized clinical trials (RCT) have shown that CPP-ACP added to sugar-free chewing gums, [78] tooth paste [79] or dental cream [80,81] increased enamel subsurface remineralization. These RCT results suggested both a short-term remineralization effect of CPP-ACP and a caries-preventing effect for long-term clinical CPP-ACP use [82]. A recent study has demonstrated that CPP could be detected on the tooth surface 3hours after chewing sugar free gum containing CPP ACP. Recaldent is an active ingredient derived from caesin, part of protein found in cow's milk. It works safely; strengthen teeth by delivering calcium and phosphate in a unique soluble form to remineralize enamel. Recaldent will not affect people with lactose intolerance. The acid resistance of enamel lesions remineralization in situ by a sugar free chewing gum containing CPP ACP is similar to gum not containing CPP ACP [83]. Cai et al. [84] demonstrated the effect of CPP ACP incorporated into a sugar free lozenges on enamel remineralization in a human in situ model.

Conclusion

We have a variety of new agents which can be used to prevent dental caries but application of these agents in clinical trials is still limited in the developing countries. Moreover dental caries is a multi-factorial and all non-fluoride measures should be evaluated properly in human trials so that they can be introduced at the community level for the prevention of dental caries.

References

1. Selwitz RH, Ismail AI, Pitts NB (2007) Dental caries. Lancet 369: 51-59.
2. Singh ML, Papas AS (2009) Long-term clinical observation of dental caries in salivary hypofunction patients using a supersaturated calcium-phosphate remineralizing rinse. J Clin Dent 20: 87-92.
3. Dawes C (1989) Fluorides: mechanisms of action and recommendations for use. J Can Dent Assoc 55: 721-723.
4. Walsh T, Worthington HV, Glenny AM, Appelbe P, Marinho VC, et al. (2010) Fluoride toothpastes of different concentrations for preventing dental caries in children and adolescents. Cochrane Database Syst Rev: CD007868.
5. American Dental Association Council on Scientific Affairs (2006) Professionally applied topical fluoride: evidence-based clinical recommendations. J Am Dent Assoc 137: 1151-1159.
6. (2001) Recommendations for using fluoride to prevent and control dental caries

- in the United States. Centers for Disease Control and Prevention. MMWR Recomm Rep 50: 1-42.
7. Ahovuo-Saloranta A, Hiiri A, Nordblad A, Mäkelä M, Worthington HV (2008) Pit and fissure sealants for preventing dental decay in the permanent teeth of children and adolescents. *Cochrane Database Syst Rev*: CD001830.
 8. Beauchamp J, Caufield PW, Crall JJ, Donly K, Feigal R, Gooch B (2008) Evidence-based clinical recommendations for the use of pit-and-fissure sealants: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc* 139: 257-268.
 9. Roberts AJ (1995) Role of models in assessing new agents for caries prevention--non-fluoride systems. *Adv Dent Res* 9: 304-311.
 10. Ripa LW (1989) Clinical studies of high-potency fluoride dentifrices: a review. *J Am Dent Assoc* 118: 85-91.
 11. Mullen J; European Association for Paediatric Dentistry (2005) History of water fluoridation. *Br Dent J* 199: 1-4.
 12. Dental public health, Introduction to Community Dental Health: Slack.
 13. Aas JA, Griffen AL, Dardis SR, Lee AM, Olsen I, et al. (2008) Bacteria of dental caries in primary and permanent teeth in children and young adults. *J Clin Microbiol* 46: 1407-1417.
 14. Becker MR, Paster BJ, Leys EJ, Moeschberger ML, Kenyon SG, et al. (2002) Molecular analysis of bacterial species associated with childhood caries. *J Clin Microbiol* 40: 1001-1009.
 15. Bowden GH (1984) Possibilities for modifying the caries attack by altering the oral microflora. *J Can Dent Assoc* 50: 169-172.
 16. Dawes C, Dibdin GH (2001) Salivary concentrations of urea released from a chewing gum containing urea and how these affect the urea content of gel-stabilized plaques and their pH after exposure to sucrose. *Caries Res* 35: 344-353.
 17. Dibdin GH, Dawes C (1998) A mathematical model of the influence of salivary urea on the pH of fasted dental plaque and on the changes occurring during a cariogenic challenge. *Caries Res* 32: 70-74.
 18. Kleinberg I (1967) Effect of urea concentration on human plaque pH levels in situ. *Arch Oral Biol* 12: 1475-1484.
 19. Burne RA, Marquis RE (2000) Alkali production by oral bacteria and protection against dental caries. *FEMS Microbiol Lett* 193: 1-6.
 20. Van Wuyckhuysse BC, Perinpanayagam HE, Bevacqua D, Raubertas RF, Billings RJ, et al. (1995) Association of free arginine and lysine concentrations in human parotid saliva with caries experience. *J Dent Res* 74: 686-690.
 21. Margolis HC, Duckworth JH, Moreno EC (1988) Composition of pooled resting plaque fluid from caries-free and caries-susceptible individuals. *J Dent Res* 67: 1468-1475.
 22. Stephan RM (1944) Intra-oral hydrogen-ion concentration associated with dental caries activity. *J Dent Res* 23: 257-266.
 23. Turtola LO, Luoma H (1972) Plaque pH in caries-active and inactive subjects modified by sucrose and fluoride, with and without bicarbonate-phosphate. *Scand J Dent Res* 80: 334-343.
 24. Wolinsky LE, Mania S, Nachnani S, Ling S (1966) The inhibiting effect of aqueous *Azadirachta indica* (Neem) extract upon bacterial properties influencing *in vitro* plaque formation. *J Dent Res*. 75(2):816-822.
 25. Agarwal P, Nagesh L, Murlikrishnan (2010) Evaluation of the antimicrobial activity of various concentrations of Tulsi (*Ocimum sanctum*) extract against *Streptococcus mutans*: an *in vitro* study. *Indian J Dent Res*. 21(3):357-359.
 26. Seneviratne CJ, Wong RW, Hägg U, Chen Y, Herath TD, et al. (2011) Prunus mume extract exhibits antimicrobial activity against pathogenic oral bacteria. *Int J Paediatr Dent* 21: 299-305.
 27. Ferrazzano A, Taylor PW, Hamilton-Miller JM, Stapleton PD (2005) Antimicrobial properties of green tea catechins. *Food Sci Technol Bull* 2: 71-81.
 28. Tagashira M, Bhattacharya, Uchiyama K, Yoshimura T, Shirota M (1997) Inhibition by hop bract polyphenols of cellular adherence and water-insoluble glucan synthesis of mutans streptococci. *Biosci Biotechnol Biochem* 61: 332-335.
 29. Ooshima T, Osaka Y, Sasaki H, Osawa K, Yasuda H, et al. (2000) Caries inhibitory activity of cacao bean husk extract in in-vitro and animal experiments. *Arch Oral Biol* 45: 639-645.
 30. Osawa K, Miyazaki K, Shimura S, Okuda J, Matsumoto M, et al. (2001) Identification of cariostatic substances in the cacao bean husk: their anti-glucosyltransferase and antibacterial activities. *J Dent Res* 80: 2000-2004.
 31. Steinberg D, Feldman M, Ofek I, Weiss EI (2004) Effect of a high-molecular-weight component of cranberry on constituents of dental biofilm. *J Antimicrob Chemother* 54: 86-89.
 32. Koo H, Xiao J, Klein MI, Jeon JG (2010) Exopolysaccharides produced by *Streptococcus mutans* glucosyltransferases modulate the establishment of microcolonies within multispecies biofilms. *J Bacteriol* 192: 3024-3032.
 33. Yamanaka A, Kimizuka R, Kato T, Okuda K (2004) Inhibitory effects of cranberry juice on attachment of oral streptococci and biofilm formation. *Oral Microbiol Immunol* 19: 150-154.
 34. Koo H, Pearson SK, Scott-Anne K, Abranches J, Cury JA, et al. (2002) Effects of apigenin and *tt*-farnesol on glucosyltransferase activity, biofilm viability and caries development in rats. *Oral Microbiol Immunol* 17: 337-343.
 35. Koo H, Schobel B, Scott-Anne K, Watson G, Bowen WH, et al. (2005) Apigenin and *tt*-farnesol with fluoride effects on *S. mutans* biofilms and dental caries. *J Dent Res* 84: 1016-1020.
 36. Darout IA, Albandar JM, Skaug N, Ali RW (2002) Salivary microbiota levels in relation to periodontal status, experience of caries and miswak use in Sudanese adults. *J Clin Periodontol* 29: 411-420.
 37. Almas K, Al-Zeid Z (2004) The immediate antimicrobial effect of a toothbrush and miswak on cariogenic bacteria: a clinical study. *J Contemp Dent Pract* 5: 105-114.
 38. Ramakrishna Y, Goda H, Baliga MS, Munshi AK (2011) Decreasing cariogenic bacteria with a natural, alternative prevention therapy utilizing phytochemistry (plant extracts). *J Clin Pediatr Dent* 36: 55-63.
 39. Ikeno K, Ikeno T, Miyazawa C (1991) Effects of propolis on dental caries in rats. *Caries Res* 25: 347-351.
 40. Duailibe SA1, Gonçalves AG, Ahid FJ (2007) Effect of a propolis extract on *Streptococcus mutans* counts *in vivo*. *J Appl Oral Sci* 15: 420-423.
 41. Koo H, Rosalen PL, Cury JA, Park YK, Ikegaki M, et al. (1999) Effect of *Apis mellifera* propolis from two Brazilian regions on caries development in desalivated rats. *Caries Res* 33: 393-400.
 42. Li XC, Cai L, Wu CD (1997) Antimicrobial compounds from *Ceanothus americanus* against oral pathogens. *Phytochemistry* 46: 97-102.
 43. Xie Q, Li J, Zhou X (2008) Anticaries effect of compounds extracted from *Galla chinensis* in a multispecies biofilm model. *Oral Microbiol Immunol* 23: 459-465.
 44. Greenberg M, Dodds M, Tian M (2008) Naturally occurring phenolic antibacterial compounds show effectiveness against oral bacteria by a quantitative structure-activity relationship study. *J Agric Food Chem* 56: 11151-11156.
 45. Loesche WJ, Grossman NS, Earnest R, Corpron R (1984) The effect of chewing xylitol gum on the plaque and saliva levels of *Streptococcus mutans*. *J Am Dent Assoc* 108: 587-592.
 46. Svanberg M, Birkhed D (1991) Effect of dentifrices containing either xylitol and glycerol or sorbitol on mutans streptococci in saliva. *Caries Res* 25: 449-453.
 47. Vadeboncoeur C, Trahan L, Mouton C, Mayrand D (1983) Effect of xylitol on the growth and glycolysis of acidogenic oral bacteria. *J Dent Res* 62: 882-884.
 48. Arends J, Smits M, Ruben JL, Christoffersen J (1990) Combined effect of xylitol and fluoride on enamel demineralization *in vitro*. *Caries Res* 24: 256-257.
 49. Isokangas P (1987) Xylitol chewing gum in caries prevention. A longitudinal study on Finnish school children. *Proc Finn Dent Soc* 83: 1-117.
 50. Alanen P, Isokangas P, Gutmann K (2000) Xylitol candies in caries prevention: results of a field study in Estonian children. *Community Dent Oral Epidemiol* 28: 218-224.
 51. Honkala E, Honkala S, Shyama M, Al-Mutawa SA (2006) Field trial on caries prevention with xylitol candies among disabled school students. *Caries Res* 40: 508-513.
 52. Oscarson P, Lif Holgersson P, Sjöström I, Twetman S, Stecksén-Blicks C (2006) Influence of a low xylitol-dose on mutans streptococci colonisation and caries development in preschool children. *Eur Arch Paediatr Dent* 7: 142-147.

53. Milgrom P, Ly KA, Tut OK, Mancl L, Roberts MC, et al. (2009) Xylitol pediatric topical oral syrup to prevent dental caries: a double-blind randomized clinical trial of efficacy. *Arch Pediatr Adolesc Med* 163: 601-607.
54. Sintes JL, Elias-Boneta A, Stewart B, Volpe AR, Lovett J (2002) Anticaries efficacy of a sodium monofluorophosphate dentifrice containing xylitol in a dicalcium phosphate dihydrate base. A 30-month caries clinical study in Costa Rica. *Am J Dent* 15: 215-219.
55. Sintes JL, Escalante C, Stewart B, McCool JJ, Garcia L, et al. (1995) Enhanced anticaries efficacy of a 0.243% sodium fluoride/10% xylitol/silica dentifrice: 3-year clinical results. *Am J Dent* 8: 231-235.
56. Tanboga I, Çaglar E, Kargul B (2003) Campaign of probiotic food consumption in Turkish children, oral perspectives 'Probiotics for your child'. *Int J Pediatr Dent* 13: 59-64.
57. Caglar E, Holcomb, Kargul B, Tanboga I (2005) Bacteriotherapy and probiotics' role on oral health. *Oral Dis* 11: 131-137.
58. Comelli EM, Guggenheim B, Stingle F, Neeser JR (2002) Selection of dairy bacterial strains as probiotics for oral health. *Eur J Oral Sci* 110: 218-224.
59. Ahola AJ, Yli-Knuutti H, Suomalainen T, Poussa T, Ahlström A, et al. (2002) Short-term consumption of probiotic-containing cheese and its effect on dental caries risk factors. *Arch Oral Biol* 47: 799-804.
60. Caglar E, Cildir SK, Ergeneli S, Sandalli N, Twetman S (2006) Salivary mutans streptococci and lactobacilli levels after ingestion of the probiotic bacterium *Lactobacillus reuteri* ATCC 55730 by straws or tablets. *Acta Odontol Scand* 64: 314-318.
61. Wolf BW, Garleb KA, Ataya DG, Casas IA (1995) Safety and tolerance of *Lactobacillus reuteri* in healthy adult male subjects. *Microb Ecol Health Dis* 8: 41-50.
62. Caglar E, Kuscu OO, Cildir SK, Kuvvetli SS, Sandalli N (2008) A probiotic lozenge administered medical device and its effect on salivary mutans streptococci and lactobacilli. *Int J Paediatr Dent* 18: 35-39.
63. Allan I, Newman H, Wilson M (2001) Antibacterial activity of particulate bioglass against supra- and subgingival bacteria. *Biomaterials* 22: 1683-1687.
64. Marinho VC, Higgins JP, Sheiham A, Logan S (2003) Fluoride toothpastes for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev* 1: CD002278.
65. Allaudin SS, Fontana M (2006) Evaluation of Novamin as an adjunct to fluoride for caries lesion remineralization. *Novamin Research Report*.
66. KG Chhabra, Preetha J Shetty, Prasad KVV, Chaya S Mendon, Ramya Kalyanpur. (2011) The beyond measures: Non fluoride preventive measures for dental caries. *JIOH* 3: 1-7.
67. Marsh PD (2010) Controlling the oral biofilm with antimicrobials. *J Dent* 38 Suppl 1: S11-15.
68. Oatmen RT. Preventive Dentistry Techniques in the Treatment of Dental Caries and Biofilm Control: A Review. Honors Projects. Undergraduate Research and Creative Practice.
69. Autio-Gold J (2008) The role of chlorhexidine in caries prevention. *Oper Dent* 33: 710-716.
70. Jenkins S, Addy M, Newcombe R (1991) Triclosan and sodium lauryl sulphate mouthwashes (I). Effects on salivary bacterial counts. *J Clin Periodontol* 18: 140-144.
71. Kulkarni VV, Damle SG (2003) Comparative evaluation of efficacy of sodium fluoride, chlorhexidine and triclosan mouth rinses in reducing the mutans streptococci count in saliva: an *in vivo* study. *J Indian Soc Pedod Prev Dent* 21: 98-104.
72. Shapiro S, Guggenheim B (1995) The action of thymol on oral bacteria. *Oral Microbiol Immunol* 10: 241-246.
73. Glass RL, Rothman KJ, Espinal F, Vélez H, Smith NJ (1973) The prevalence of human dental caries and water-borne trace metals. *Arch Oral Biol* 18: 1099-1104.
74. Reynolds EC (1998) Anticariogenic complexes of amorphous calcium phosphate stabilized by casein phosphopeptides: a review. *Spec Care Dentist* 18: 8-16.
75. Reynolds EC (1987) The prevention of sub-surface demineralization of bovine enamel and change in plaque composition by casein in an intra-oral model. *J Dent Res* 66: 1120-1127.
76. Reynolds E (2007) Calcium phosphopeptide complexes.
77. Azarpazhooh A, Limeback H (2008) Clinical efficacy of casein derivatives: a systematic review of the literature. *J Am Dent Assoc* 139: 915-924.
78. Morgan MV, Adams GG, Bailey DL, Tsao CE, Fischman SL, et al. (2008) The anticariogenic effect of sugar-free gum containing CPP-ACP nanocomplexes on approximal caries determined using digital bitewing radiography. *Caries Res* 42: 171-184.
79. Rao SK, Bhat GS, Aradhya S, Devi A, Bhat M (2009) Study of the efficacy of toothpaste containing casein phosphopeptide in the prevention of dental caries: a randomized controlled trial in 12- to 15-year-old high caries risk children in Bangalore, India. *Caries Res* 43: 430-435.
80. Andersson A, Skold-Larsson K, Hallgren A (2007) Effect of a dental cream containing amorphous cream phosphate complexes on white spot lesion regression assessed by laser fluorescence. *Oral Health Prev Dent* 5: 229-233.
81. Bailey DL, Adams GG, Tsao CE, Hyslop A, Escobar K, et al. (2009) Regression of post-orthodontic lesions by a remineralizing cream. *J Dent Res* 88: 1148-1153.
82. Yengopal V, Mickenautsch S (2009) Caries preventive effect of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP): a meta-analysis. *Acta Odontol Scand* 67: 321-332.
83. Iijima Y, Cai F, Shen P (2004) Acid resistance of enamel subsurface lesions remineralized by a sugar free chewing gum containing casein phosphopeptide-amorphous calcium phosphate. *Caries Res* 38: 551-56.
84. Cai F, Shen P, Morgan MV, Reynolds EC (2003) Remineralization of enamel subsurface lesions *in situ* by sugar-free lozenges containing casein phosphopeptide-amorphous calcium phosphate. *Aust Dent J* 48: 240-243.

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